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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1649	

NOTIFICATION DATE	DELIVERY MODE
07/09/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/659,295	SCHAEBITZ ET AL.	
	Examiner	Art Unit	
	STACEY MACFARLANE	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 April 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,5-7,9,12,14,18,19 and 105-108* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,5-7,9,12,14,18,19 and 105-108* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

1. Claims 1, 19, 105 and 106 have been amended, claims 11, 16, 17 and 109-113 are cancelled as requested in the amendment filed on April 24, 2009. Following the amendment, claims 1, 5-7, 9, 12, 14, 18, 19 and 105-108 are pending in the instant application and are under examination in the instant office action.

2. Any objection or rejection of record, which is not expressly repeated in this action has been overcome by Applicant's response and withdrawn.

3. Applicant's arguments filed on April 24, 2009 have been fully considered but they are not deemed to be persuasive for the reasons set forth below.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Rejection of Claim 113, now cancelled, under 35 U.S.C. 112, second paragraph, is withdrawn.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1, 5-7, 9, 12, 14, 18, 19 and 105-108 stand as rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement for reasons of record in the Office action mailed March 27, 2009.

On page 5 of Remarks filed April 24, 2009, Applicant traverses on the grounds that the claim amendments limiting the language of the claim to G-CSF or "a protein having at least 90% homology to SEQ ID NO: 28 and G-CSF activity", in view of the art at the time of filing indicating G-CSF was a well-known factor, obviate the rejection. This has been considered in full but is not found persuasive for the following reasons.

While G-CSF was well-known in the art at the time of filing and SEQ ID NO: 28 is a clearly defined amino acid sequence, those proteins having at least 90% homology to SEQ ID NO: 28 and G-CSF activity are not clearly defined within the art, nor are they described within the instant specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. SEQ ID NO: 28 is a 207 amino acid protein and claims encompass proteins in which any 20 of those amino acids are altered and yet the protein maintains "G-CSF activity".

With respect to the description of substituted G-CSF the specification provides several specific examples but the claims are more broadly encompassing:

> Lysine altered proteins as described in U.S. Pat. No. 4,904,584; cysteine altered variants of proteins as described in WO/9012874 (U.S. Pat. No. 5,166,322); the addition of amino acids to either terminus of a GCSF molecule for the purpose of aiding in the folding of the molecule after prokaryotic expression as described in AU-A-10948/92; substituting the sequence Leu-Gly-His-Ser-Leu-Gly-Ile (SEQ ID NO:11) at position 50-56 of GCSF with 174 amino acids (SEQ ID NO:37), and position 53 to 59 of the GCSF with 177 amino acids (SEQ ID NO:39), or/and at least one of the four histadine residues at positions 43, 79, 156 and 170 of the

> mature GCSF with 174 amino acids (SEQ ID NO:37) or at positions 46, 82, 159, or 173 of the mature GCSF with 177 amino acids (SEQ ID NO:39) as described in AU-A-76380/91. [0057]

The description goes on to describe assay methods for screening said proteins for the biological activity of GCSF (paragraph [0059]).

In order to provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The court has stated that compliance with the written description requirement is a question of fact. "A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *University of California v. EliLilly and Co.*, 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1405 (Fed. Cir. 1997 (bracketed material in original). The claims in the *Lilly* case were directed generically to vertebrate or mammalian insulin cDNAs and the court held that a structural description of a rat cDNA was not an adequate description of these broader classes of cDNAs See id. at 1567, 43 USPQ2d at 1405. The standard applies to proteins as well as DNA. *See University of Rochester v. G.D. Searle & Co., Inc.*, 358 F.3d 916, 925, 69 USPQ2d 1886, "893 (Fed. Cir. 2004).

The Lilly court explained that claims encompassing mammalian cDNA with insulin activity without more description is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function. It does not specifically define any of the molecules that fall within its definition,

nor does it define any structural features commonly possessed by members of the genus that distinguish them from others. Thus, one skilled in the art cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. *Id*. at 1568, 43 USPQ2d at 1406. The Lilly court set out that a genus could be described by means of a recitation of a representative number of molecules, defined by sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus. *Id*. at 1569.

In the instant case, the only factor present in the claim is a recitation of a requisite % homology and an activity. There is not even identification of any particular portion or core structure within human G-CSF or SEQ ID NO: 28 that must be conserved for said activity. Examiner maintains the position that the claims encompass proteins with unknown structure and, thus, are drawn to genera of molecules defined merely by activity (e.g. "G-CSF activity"). The instant specification fails to describe the entire genera of molecules that are encompassed by these claims by failing to provide any distinguishing characteristics in the form of structure or structure-to-function correlation. It is not even clear what molecules, even from those specifically recited in paragraph [0057], retain the requisite "G-CSF activity". Therefore, just as in *University of Rochester*, the present specification does not disclose which peptides having 90% homology to SEQ ID NO: 28 fulfill the functional limitation. Furthermore, the specification fails to provide a representative number of species for the recited genus.

Granted, those skilled in the art could screen libraries of proteins having at least 90% homology to SEQ ID NO: 28. That, however, does not make up for the deficiency of the specification's description. The *University of Rochester* court specifically noted that the patent at issue there disclosed screening assays to identify compounds having the desired activity, but nonetheless held that the description was inadequate. The same holds true here. Thus, the rejection is maintained.

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. As currently amended, Claims 1, 9 and 19 are rejected under 35 U.S.C. 102(b) as being anticipated by Whalen *et al.*, 1999 cited in the Office action mailed March 27, 2009.

10. As amended claims are drawn to a method of treating traumatic brain injury in a mammal comprising administering human G-CSF or a protein having at least 90% homology to SEQ ID NO: 28 (identified as human G-CSF) and assessing neurological function after said administering.

The instant disclosure provides no explicit definition for “neurological function” of the claims, nor does the disclosure provide guidance as to what specific assessments are to be performed in order to successfully assess function post-TBI. The disclosure

only provides description for the measurement of regional cerebral blood flow, infarct volume, sensory-motor function and behavioral testing following ischemia or thomboembolic stroke in animal models; and assessing survival in an ALS animal model. Therefore, the assessment of neurological function following administration of G-CSF is given the broadest reasonable interpretation within the art and encompasses any assessment of neurophysiology or nervous system function following administration.

The Whalen et al. prior art teaches a method for treating traumatic brain injury comprising administering recombinant human G-CSF (page 3711, paragraph bridging columns 1 and 2) subcutaneously (page 3711, section entitled *Experimental Group*, line 13) and assessing neurological function following administration. Specifically, the Whalen prior art uses a rat model for TBI consisting of a controlled cortical impact (CCI). Whalen et al. teach assessing neurological function as measured by blood-brain barrier permeability (Figure 1B) and percent brain water as an indication of brain edema (Figure 2B). Therefore, the method of the instant claims fails to distinguish over that of the prior art.

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. Claims 5-7 are as rejected under 35 U.S.C. 103(a) as being unpatentable over Whalen et al. as applied to claims 1, 9 and 19 above, and further in view of Brines et al. (2000) cited in the Office action mailed May 22, 2008.

The Whalen et al. prior art teaches a method for treating traumatic brain injury in a mammal comprising administering recombinant human G-CSF subcutaneously and assessing neurological function as measured by blood-brain barrier permeability and percent brain water or brain edema.

The Whalen et al. reference does not teach the method further comprising administering one or more additional hematopoietic factors, nor specifically erythropoietin as required by instant claims 5, 6, and 7, however, the Brine et al. reference, however, teaches that methods for the treatment of traumatic brain injury comprising administering erythropoietin were well-known in the art prior to filing.

Section 2144.06 of the MPEP provides guidance as to obviousness of art recognized equivalence for the same purpose. The court has stated, "It is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980).

Therefore, the invention as a whole is *prima facie obvious*, if not actually anticipated by the reference.

13. Claim 12 is rejected under 35 U.S.C. 103(a) as being unpatentable over Whalen et al. as applied to claims 1, 9 and 19 above, and further in view of Deleuze (2000) cited in the Paper mailed May 22, 2008.

The Whalen et al. prior art teaches a method for treating traumatic brain injury in a mammal comprising administering recombinant human G-CSF subcutaneously and assessing neurological function as measured by blood-brain barrier permeability and percent brain water or brain edema.

The Whalen et al. reference does not teach the method further comprising administering tissue plasminogen activator as required by instant claim 12. The Deleuze reference, however, teaches treatments of traumatic brain injury comprising administration of tissue plasminogen activator were known in the art. Since the *Kerkhoven* case law (*Id.*) states that it is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, the invention as a whole is *prima facie obvious*, if not actually anticipated by the reference.

14. Claim 14 is rejected under 35 U.S.C. 103(a) as being unpatentable over Whalen et al. as applied to claims 1, 9 and 19 above, and further in view of Morita-Fujimura (1999) cited in the Paper mailed May 22, 2008.

The Whalen et al. prior art teaches a method for treating traumatic brain injury in a mammal comprising administering recombinant human G-CSF subcutaneously and

assessing neurological function as measured by blood-brain barrier permeability and percent brain water or brain edema.

The Whalen et al. reference does not teach the method further comprising an anti-apoptotic agent defined within the specification as "e.g. inhibitors of caspases". However, Morita-Fujimura et al. teach the administration of inhibitors of caspases for the treatment of traumatic brain injury in mammals was known in the art prior to filing. Therefore, the invention as a whole is *prima facie obvious*, if not actually anticipated by the reference.

15. Claims 105-108 are rejected under 35 U.S.C. 103(a) as being unpatentable over Whalen et al. as applied to claims 1, 9 and 19 above, and further in view of Neupogen® (Filgrastim) Amgen product information sheet dated 1998 and previously cited in the Office Action mailed November 10, 2008.

The Whalen et al. prior art teaches a method for treating traumatic brain injury in a mammal comprising administering recombinant human G-CSF subcutaneously and assessing neurological function as measured by blood-brain barrier permeability and percent brain water or brain edema.

The Whalen et al. reference does not teach the method comprising intravenous administration. The product information published prior to filing by the maker of commercially available human GCSF, Amgen, indicate that Filgrastim could be interchangeably administered by oral, intravenous, subcutaneous, or intraperitoneal routes with no significant difference in effect. In *KSR International Co. v. Teleflex, Inc.,*

the Supreme Court has stated that where there is a "pressure to solve a problem and a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense" (*KSR International Co. v. Teleflex, Inc.* 127 S. Ct. 1727, 82 USPQ2d 1385, Supreme Court, April 30, 2007).

In the instant case, the problem to be solved is the route of administration and the art demonstrates that there are a finite number of ways to administer and does not indicate any differing or unexpected effects by either route. Therefore, it would have been obvious to one of ordinary skill in the art to combine the method as taught by Whalen et al., with the routes of administration as taught by the product manufacturer and the invention as a whole is *prima facie* obvious if not anticipated by the prior art.

Conclusion

16. No Claim is allowed.

17. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not

mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to STACEY MACFARLANE whose telephone number is (571)270-3057. The examiner can normally be reached on M-W and F 5:30 to 2, TELEWORK-Thursdays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker can be reached on (571) 272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Stacey MacFarlane

Examiner
Art Unit 1649

/John D. Ulm/
Primary Examiner, Art Unit 1649